

Abstracts

Major Motor Drop Seizures for Endpoint Assessments in a Phase 3 Trial of Soticlestat in Individuals with Lennox–Gastaut Syndrome

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Rationale: Over the past 20 years, interventional clinical trials for the treatment of Lennox–Gastaut syndrome (LGS) have typically included assessment of drop seizures as a primary efficacy outcome measure. Drop seizures are usually brief and may involve the whole body, just the head, or other body areas. In clinical trials, parents and caregivers are asked to report drop seizures based on their assessment of whether a seizure leads to a drop, or would have led to a drop if the trial participant was standing. As such, some drop seizures may be difficult

to identify and classify, and the term may be interpreted quite broadly. Ideally, an outcome measure for seizure assessment should be clinically relevant, easily identifiable, and reliably counted by the parent or caregiver across all study sites. Based on favorable efficacy, safety, and tolerability data from the phase 2 ELEKTRA study (NCT03650452), soticlestat is being investigated further as adjunctive therapy for children and adults with LGS and Dravet syndrome. To reduce potential variability in drop seizure assessments in upcoming phase 3 clinical studies in LGS, we sought to develop a new operational definition for drop seizures.

Methods: In consultation with researchers in the epilepsy field and epileptologists and considering the International League Against Epilepsy (ILAE) seizure classification, an updated term for drop seizures was developed to include as an outcome measure in a phase 3 study of soticlestat in individuals with LGS, and its open-label extension (OLE) study.

Results: The term 'major motor drop' (MMD) seizure will be used as the primary outcome measure to assess efficacy in a phase 3 study of soticlestat in individuals with LGS, and as a secondary outcome in the OLE study. MMD seizures will be identified based on ILAE seizure classification categories and observation of the body areas involved. Focal-onset, generalized-onset and unknown-onset motor seizures involving the major body areas, such as the lower extremities or trunk, leading to or likely leading to a fall, will be considered MMD seizures. Motor seizures such as isolated head drops or involving only the face and arms will not be considered MMD seizures.

Conclusions: Introduction of the term MMD seizures in the clinical trial setting may reduce variability by providing a more accurate operational definition for countable drop seizures. Accordingly, consistent reporting by parents, caregivers and investigators should lead to a more accurate and reliable measure of the efficacy of antiseizure medications for the treatment for LGS.

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Categories : Anti-seizure Medications

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